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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,046	09/09/2005	Harald Schlebusch	14836-46758	8798

24728 7590 10/03/2006

MORRIS MANNING MARTIN LLP
3343 PEACHTREE ROAD, NE
1600 ATLANTA FINANCIAL CENTER
ATLANTA, GA 30326

EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/507,046	SCHLEBUSCH ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☒ Claim(s) *7-11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The response filed on 9/6/06 to the restriction requirement of 8/7/06 has been received. Applicant has elected Group I for examination without traverse.

Claims 1-12 were pending.

Claim 12 has been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 1-11 are currently under consideration.

Claim Objections

Claims 7-11 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend upon another multiple dependent claim. See MPEP § 608.01(n). Accordingly, claims 7-11 have not been further treated on the merits.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 3-5 are rejected under 35 U.S.C. 101 because the claims, as written, do not sufficiently distinguish over anti-anti-idiotypic antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the

absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention appears to employ novel biological materials, specifically monoclonal anti-idiotypic antibody ACA125 produced by the hybridoma 3D5 (DSM ACC2120). Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record

over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of the deposit will be made (see 37 C.F.R. 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to M.P.E.P. 2400 in general, and specifically to 2411.05, as well as 37 C.F.R. 1.809(d), wherein it is set forth that the "specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended

to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the

invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986)..

The claims are broadly drawn to an anti-anti-idiotypic antibody that reacts with an anti-idiotypic antibody which represents an internal image of the antigen CA125, is specific for the tumour-associated antigen CA125 and reacts with this antigen, and mediates an antibody-dependent cellular cytotoxicity against CA-125-expressing tumour cells.

The specification discloses that ovarian carcinoma patients were immunized with the anti-idiotypic antibody ACA125 (Ab2), which induced the production of specific anti-anti-idiotypic Ab3 antibodies against said Ab2 (pages 7-8, in particular). Whereas Ab3 antibodies bind to the anti-idiotypic antibody Ab2, such antibodies do no bind to the corresponding antigen, in this case CA-125 (page 3, in particular). The instant claims are drawn to Ab1' antibodies, which can bind to anti-idiotypic antibody Ab2 as well as to the original antigen (CA-125). The specification asserts that said Ab1' antibodies against CA-125 are also able to mediate an antibody-dependent cellular cytotoxicity against CA-125 expressing tumour cells (see pending claims 1-6 and page 3, in particular). The specification discloses that patients immunized with the anti-idiotypic antibody ACA125 (Ab2) produced Ab1' antibodies (pages 8-9, in particular). The specification further discloses that OAW-42 is an ovarian carcinoma cell line that expresses CA-125 and SKOV-3 is an ovarian carcinoma cell line that does not express CA-125 (page 8, in particular). The specification does not disclose any of the other differences between OAW-42 cells and SKOV-3 cells, including differences in cell

survival regulation between the two different cell lines. Further, the specification discloses that treatment with postantiserum from patients that generated Ab1' antibodies induced cell death of OAW-42 cells, but did not significantly affect the viability of SKOV-3 cells (Figure 2, in particular).

In regards to the claimed Ab1 antibodies being able to mediate an antibody-dependent cellular cytotoxicity against CA125- expressing tumor cells *in cell culture*, one of skill in the art would recognize that the disclosed comparison of cell survival after treating two different cell types with serum comprising Ab1' antibodies for CA-125 does not take into account whether differences other than the CA-125 status of said cells influenced cell viability after serum treatment. One of skill in the art would recognize that there are multiple signaling pathways which mediate cell survival, and it is unclear whether differences other than the CA-125 status of OAW-42 cells and SKOV-3 cells influenced cell viability after said serum treatment. Further, the disclosed experiments with OAW-42 cells and SKOV-3 cells did not use purified Ab1' antibody. Therefore, it is unclear whether Ab1' antibody or something else in the serum increased the death of OAW-42 cells, as compared to OAW-42 cells treated with preantisera.

In regards to the claimed Ab1 antibodies mediating an antibody-dependent cellular cytotoxicity against CA125- expressing tumor cells *in vivo*, one of skill in the art would recognize that therapeutic cancer treatments, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated

with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re* Brana (34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claim is not drawn to an anti-anti-idiotypic antibody which has known in vivo ability to mediate an antibody-dependent cellular cytotoxicity against CA125-expresssing cells. Further, the instant specification provides no in vivo data, particularly demonstrating that the claimed anti-anti-idiotypic antibody would predictably mediate an antibody-dependent cellular cytotoxicity against CA125-expresssing cells in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of a specific cancer enables compositions for specific therapeutic effects in humans and does not require human clinical testing; however, the instant application is claiming an anti-anti-idiotypic antibody that provides a therapeutic effect without providing any in vivo data, hence the claimed

invention is not enabled. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as immunotherapy.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the anti-anti-idiotypic antibody would function as claimed (either in cell culture or in vivo).

Summary

No claim is allowed. Claims 7-11 are objected to and have not been further treated on the merits. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching an anti-anti-idiotypic antibody that reacts with an anti-idiotypic antibody which represents an internal image of the antigen CA125, is specific for the tumour-associated antigen CA125 and reacts with this antigen, and mediates an antibody-dependent cellular cytotoxicity against CA-125-expressing tumour cells. The closest prior art for claims 1-6 is Wagner et al (US Patent 5,858,361, 1/12/99), which teaches an anti-anti-idiotypic antibody that reacts with an anti-idiotypic antibody which represents an internal image of the antigen CA125 and may be specific for the tumour-associated antigen CA125; however, this reference does not teach or suggest an anti-anti-idiotypic antibody that reacts with an anti-idiotypic antibody which represents an internal image of the antigen CA125, is specific for the tumour-associated antigen

CA125 and reacts with this antigen, and mediates an antibody-dependent cellular cytotoxicity against CA-125-expressing tumour cells.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

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